REMARKS/ARGUMENTS

Claims 1-16 are currently pending in the above-identified application. Claims 1-14 have been withdrawn from consideration by the Examiner as not pertaining to an elected invention. Claims 15 and 16 have been amended. Support for these amendments is identified in the following remarks. Further, new claims 17 through 24 have been added. Support for the new claims is identified in the following remarks. No new matter is added by these amendments or the new claims.

Information Disclosure Statement

The Examiner has indicated that one item of information in the IDS form 1449 filed September 2, 2003 fails to comply with all the requirements of 37 CFR 1.97 and 37 CFR 1.98; and that this item was not considered. Applicants' representative has reviewed the IDS returned with the present office action and note that item CT designated EMBL Accession No. Q9LJL5 has not been initialed by the Examiner. The reference is a sequence abstract from the EMBL Nucleotide Database wherein the Identification No. for the item in the database was correctly designated Q9LJL5. The EMBL Nucleotide Database Identification No. is associate with the sequence information related to a protein designated cyclin-dependent kinase inhibitor 6 giving three individual references. The designation was also indicated on the International Search Report. As such Applicants believe that the reference was properly identified and that it was possible from the designation and information provided in the IDS to determine the publisher, relevant pages and place of publication as required by 37 CFR 1.97 and 37 CFR 1.98.

Although Applicants believe that the reference is properly listed as part of the September 2, 2003 IDS as set forth above, a revised 1149 is attached hereto that adds the publication date and to clearly indicate that the publication is a printout of information from the EMBL Nucleotide Database "Online". Applicants respectfully request that the reference be considered by the Examiner.

Specification

The disclosure is objected to because the Examiner believes that the specification fails to comply with 37 CFR 1.821(d), in that reference is not made to all sequences recited in the text by use of a sequence identifier preceded by "SEQ ID NO:". In particular, the Examiner has directed our attention to page 16 of the specification as filed where an amino acid sequence for a region of BRO proteins as described by Applicants is provided. The Examiner does not believe that this sequence has been properly identified with a SEQ ID NO: and the Examiner has requested correction of this asserted error.

Applicants' representative has reviewed page 16 of the specification and it should be noted that the sequence:

Lys TyrAsnPheAspXaa$_1$Xaa$_2$Xaa$_3$Xaa$_4$Xaa$_5$ProLeu

Xaa$_6$Xaa$_7$GlyArgTyrXaa$_8$TrpXaa$_9$Xaa$_{10}$LeuXaa$_{11}$

that appears at page 16 has been properly identified and designated SEQ ID NO: 10. The designation appears on page 17 following the complete definitions for Xaa$_1$ through Xaa$_{11}$. Applicants respectfully request the Examiner review page 17 of the specification where the amino acid sequence has been properly identified as SEQ ID NO: 10. Therefore, Applicants believe that the objection to the specification as failing to comply with 37 CFR 1.821(d) is unwarranted. The Examiner is respectfully requested to reconsider and withdraw the objection to the specification. Should the Examiner believe that the sequence has not been properly designated and it is preferred that the designation be relocated, Applicants will consider an amendment to the specification.

Rejections under 35 U.S.C. §112

Claim 15, and claim 16 dependent thereon, stand rejected under 35 U.S.C. §112, second paragraph, the Examiner believing that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In

particular the Examiner believes claim 15 is indefinite in the recitation of "D-like protein". The Examiner believes it is unclear in what way the encoded protein is "like" D, as one protein may be like another in more than one way, such as structure(s), function(s), localization, pathway(s), etc., and the nature of the likeness of the encoded protein to a D protein is not believed to be disclosed in the specification or evidence from the limitations recited in the claim. The Examiner also believes that it is unclear what a D protein is.

Applicants have amended claim 15 to recite "the plant D-like cyclin inhibitor protein designated BRO4". This amendment is believed to fully define the protein of the present invention as a plant D-like cyclin inhibitor protein of a particular designation and to make claim 15 consistent with other claims. Further, the amino acid sequence which is representative of the invention is also provided as an element of the claim. The Examiner is respectfully requested to reconsider and withdraw this rejection in light of the amendment of claim 15.

Rejections under 35 U.S.C. §101 and 35 U.S.C. § 112

Claims 15 and 16 stand rejected under 35 U.S.C. §101 because the Examiner does not believe that the claimed invention is supported by either a specific and substantial asserted utility or a well established utility. The Examiner has summarized the claims as being drawn to a nucleotide sequence which encodes the plant D-like protein designated BRO4 as depicted in SEQ ID NO: 8, including the nucleotide sequence depicted in SEQ ID NO: 7. Further, the Examiner describes the specification as disclosing that SEQ ID NO:7 is a partial cDNA sequence 626 nucleotides in length that encodes a 209 amino acid polypeptide of SEQ ID NO:8, and that SEQ ID NO:7 was obtained from an *Arabidopsis* library using a yeast two-hybrid system designed to screen for sequences that encode proteins that interact with the *Arabidopsis* D-type cyclin D1 (pages 25-27; sequence listing). The Examiner also has noted that the specification discloses that SEQ ID NO:8 comprises a region of approximately 22 amino acids that is substantially homologous to the mammalian cyclin-dependent kinase binding domain consensus sequence, (page 27), but the Examiner also indicates that the specification is not believed to disclose whether SEQ ID NO:7 encodes a protein having a specific function or activity. The

Examiner goes on the state that the specification further discloses that sequences encoding the protein designated BRO4 are useful for producing transgenic plant cells or plants having an increased growth rate and/or yield as a consequence of the expressed BRO4 protein binding and inactivating a plant D-like cyclin/cyclin dependent kinase complex (pages 4-5), but that the specification does not disclose how to use SEQ ID NO:7 to achieve such an effect.

The Examiner does not believe that the claimed invention is supported by a well established utility because the prior art does not teach a use for a nucleotide sequence of SEQ ID NO:7 or which encodes SEQ ID NO:8. Further, the Examiner does not believe that the claimed invention is supported by a specific and substantial asserted utility because the Examiner does not believe such a utility has been established for a nucleotide sequence of SEQ ID NO:7 or for a nucleotide which encodes SEQ ID NO:8. Nor does the Examiner believe that the disclosure that SEQ ID NO:7 encodes a polypeptide that interacts with the *Arabidopsis* D-type cyclin D1 establishes a specific and substantial utility for a nucleotide sequence of SEQ ID NO:7 or for a nucleotide sequence which encodes SEQ ID NO:8. This is because the Examiner, citing to Luban *et al.* (*Curr. Opin. Biotechnol.* 6:59-64, 1995) and Caoinigro *et al.* (*J. Biotechnol.* 103:213-225, 2003), does not believe that the detection of a protein-protein interaction in a yeast two hybrid system is necessarily indicative of a real world use for the specific coding sequence identified.

Still further, the Examiner does not believe that the disclosure that SEQ ID NO:8 comprises a region of approximately 22 amino acids that is substantially homologous to the mammalian cyclin-dependent kinase binding domain consensus sequence establishes a specific and substantial utility for a nucleotide sequence of SEQ ID NO:7 or for a nucleotide sequence which encodes SEQ ID NO:8. This is because the Examiner does not believe that the function of a protein can reliably be predicted on the basis of its structure or its homology to other known proteins. The Examiner has cited Whisstock *et al.* (*Q Rev. Biophys.* 36:307-340, 2003) to support this position. Also, the Examiner has stated that the disclosure that the sequences encoding the protein designated BRO4 are useful for producing transgenic plant cells or plants having an increased growth rate and/or yield as a consequence of the expressed BRO4 protein

binding and inactivating a plant D-like cyclin/cyclin dependent kinase complex does not establish a specific and substantial utility for a nucleotide sequence of SEQ IDS NO: 7 or for a nucleotide sequence which encodes SEQ ID NO: 8 because the effect of expressing only part of a full-length polypeptide in transgenic plants varies depending on the fragment expressed. Zhou *et al.* (*Plant J.* 35:476-489, 2003) has been cited for support for this notion in that they teach that expression of an N-terminal truncation of the *Arabidopsis* cyclin-dependent kinase inhibitor ICK-1 increases ICK-1 effects on transgenic plants, whereas expression of a C-terminal truncation of ICK1 greatly reduces or abolishes ICK1 effects on transgenic plants.

The Examiner has also rejected claims 15 and 16 under 35 U.S.C. §112, first paragraph because the Examiner does not believe that the claimed invention is supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, and because there is not support for a specific and substantial asserted utility one skilled in the art clearly would not know how to use the claimed invention.

Applicants respectfully must disagree with the Examiner's summary of the present invention and with the summary of the disclosure as filed. The Examiner is requested to review pages 25 through 28 of the specification as filed. In these pages Applicants describe, for example, the isolation and characterization of four cDNA obtained in yeast 2-hybrid screening procedures. The cDNA designated BRO4 is not characterized as being incomplete as asserted by the Examiner. On the contrary, at page 28, line 10, it is disclosed that only the cDNA for BRO1 was determined to have been incomplete. Further, SEQ ID NO: 8 is distinctly set forth as providing a protein which begins at the Met at position number 13 and terminating with the Leu residue at position number 208 of the nucleic acid sequence set frorth as SEQ ID NO: 7. (See page 27, lines 16-17). As noted by the Examiner, the amino acid sequence depicted for BRO4 includes a 22 amino acid residue amino acid sequence that is homologous with not only other plant cyclin inhibitor genes (ICK1 and FL39), but the sequence is also disclosed to be homologous with the mammalian consensus cyclin-dependent kinase binding domain. The amino acid sequences for BRO2, BRO3 and BRO4 were also noted in the specification to include a 6 amino acid sequence homologous with the cyclin binding domain. (See page 27,

lines 21-25). This region was found to be spaced approximately 17 to 20 amino acids upstream of the cdk binding domain. (See page 27, lines 23-24). It was based initially on this collection of facts and the activity of the protein in the yeast two hybrid screening system that BRO4 was identified as a plant D-like cyclin dependent kinase inhibitor.

In addition, the specification teaches that the amino acid sequence identified as SEQ ID NO: 8 shares several domains that are conserved with those of plant cyclin inhibitor proteins. These includes a region of 22 amino acids which were substantially homologous to mammalian and plant consensus cyclin-dependent kinase binding domain and a region of about 6 amino acid residues approximately 17 to twenty amino acids upstream of the cdk binding domain that is the cylcin binding domain. Further, the specification provides in the examples a demonstration using inverted repeats from both the ICK1 and BRO4 sequences that suppress the expression of the plant D-like cyclin inhibitor genes. As expected, the transgenic plants demonstrated phenotypes of increased growth. The ICK1-IR (ICK1 inverted repeat) transgenic plants demonstrated three signs of increased growth including, larger and wider leaves (both cauline and rosette), 3 to 4 carpels instead of two, and cracks in the main stem. The BRO4-IR (BRO4 inverted repeat) transgenic plants were bushier (more conflorescences and more leaves on each coflorescence), and the plants appeared to have developed this phenotype by having formed more metamers. Each of these phenotypic observations are believed to be indicative of the suppression BRO4 expression and are consistent with the molecules being a cyclin dependent kinase inhibitor.

The Examiner has characterized the specification as teaching that "sequences encoding the protein designated BRO4 are useful for producing transgenic plant cells or plants having an increased growth rate and/or yield as a consequence of the expressed BRO4 protein binding and inactivating a plant D-like cyclin/cyclin dependent kinase complex (pages 4-5)." It should be noted that the section of the summary of the invention referred to by the Examiner recites ". . . the present invention provides a method for producing transgenic plant[s] cells having an increased growth rate and/or yield as compared to a corresponding wild-type plant. The method comprises, contacting the plant cells with nucleic acid sequences which can

functionally disrupt nucleic acid sequences encoding a cyclin inhibitor protein to obtain transformed plant cells; producing from the transformed plant cells, and selecting plants which exhibit an increased growth rate or yield as compared to a wild-type plant." This method is demonstrated by the examples provided in the application as filed for both ICK1 and BRO4. Applicants have therefore provided evidence of a specific and substantial asserted utility and/or a well established utility as required under 35 U.S.C. § 101 and 35 U.S.C. § 112.

The Examiner has cited Luban *et al.* (*Curr. Opin. Biotechnol.* 6:59-64, 1995) and Caoinigro *et al.* (*J. Biotechnol.* 103:213-225, 2003) to support the proposition that the detection of a protein-protein interaction in a yeast two hybrid system is not necessarily indicative of a real world use for a specific coding sequence that may be identified. As above, Applicants have not only identified an amino acid sequence for BRO4 and the nucleic acid sequences that encode this protein, but they have also demonstrated that inverted repeat sequences amplified from the isolated nucleic acid sequences can suppress expression of BRO4 and such suppression results in a phenotype indicative of increased plant growth and/or yield as compared to a wild-type plant. Applicants have therefore not relied only on the isolation and characterization of a nucleic acid sequence identified by yeast two-hybrid screening methods but also have further characterized the molecules to demonstrate utility of the sequences.

As above, one aspect of the utility of the sequences of the invention relates to the use of nucleotide sequences that encode the BRO4 amino acid sequence are used to functionally inactivate a plant D-like cyclin inhibitor gene. This utility is demonstrated in the examples as described above. Therefore, the citation of Zhou *et al.* (*Plant J.* 35:476-489, 2003) who teach that expression of an N-terminal truncation of the *Arabidopsis* cyclin-dependent kinase inhibitor ICK-1 increases ICK-1 effects on transgenic plants, whereas expression of a C-terminal truncation of ICK1 greatly reduces or abolishes ICK1 effects on transgenic plants are not relevant to the functional inactivation of the any gene such as the BRO4 gene as set forth in the present invention. It should also be noted that the present application describes the functional inactivation of the ICK1 gene described in Zhou *et al.* demonstrating for the first time that

functional inactivation of the ICK1 gene results in a transgenic plant having a phenotype consistent with increased growth and/or yield as compared with a wild-type plant.

Applicants have demonstrated in the application as filed a specific and substantial asserted utility and/or a well established utility. The amino acid sequence and the nucleotide sequences which encode BRO4, a cyclin inhibitor protein is provided. Vectors comprising the nucleotide sequence as designated SEQ ID NO: 7, as well as host cells transformed or transfected by the vectors comprising the nucleotide sequence encoding BRO4 (SEQ ID NO: 8), including plant cells, are also provided. The amino acid sequence and/or nucleotide sequence encoding BRO4 can be used to select oligonucleotide sequences that are effective as antisense molecules, *i.e.*, inverted repeats, that can functionally suppress the expression of BRO4 resulting in transgenic plants that demonstrate a phenotype having increased size and/or yield as compared with a wild-type plant. Therefore, as Applicants have provided a specific and substantial utility and/or a well established utility, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 15 and 16 under 35 U.S.C.§ 101 and § 112, first paragraph.

Further, Applicants have added new claims 17 through 24 to encompass certain embodiments of the invention disclosed in the application but not previously claimed. Support for the new claims can be found in the specification at, for example, pages 18 through 19 and the examples.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an

early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

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